Acute Renal Failure in Type 1 Diabetes Mellitus

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MUH

A 29 year old Caucasian male

past medical history significant for type 1 diabetes mellitus confirmed with an elevated level of antibodies to glutamic acid decarboxylase (GAD)

nausea and vomiting for the last three days.

He denied any fever, chills or cold symptoms.

His home medications comprised of lantus 20 units and regular insulin.

He was recently started on canagliflozin for uncontrolled hyperglycemia and high HbA1c (9.1).

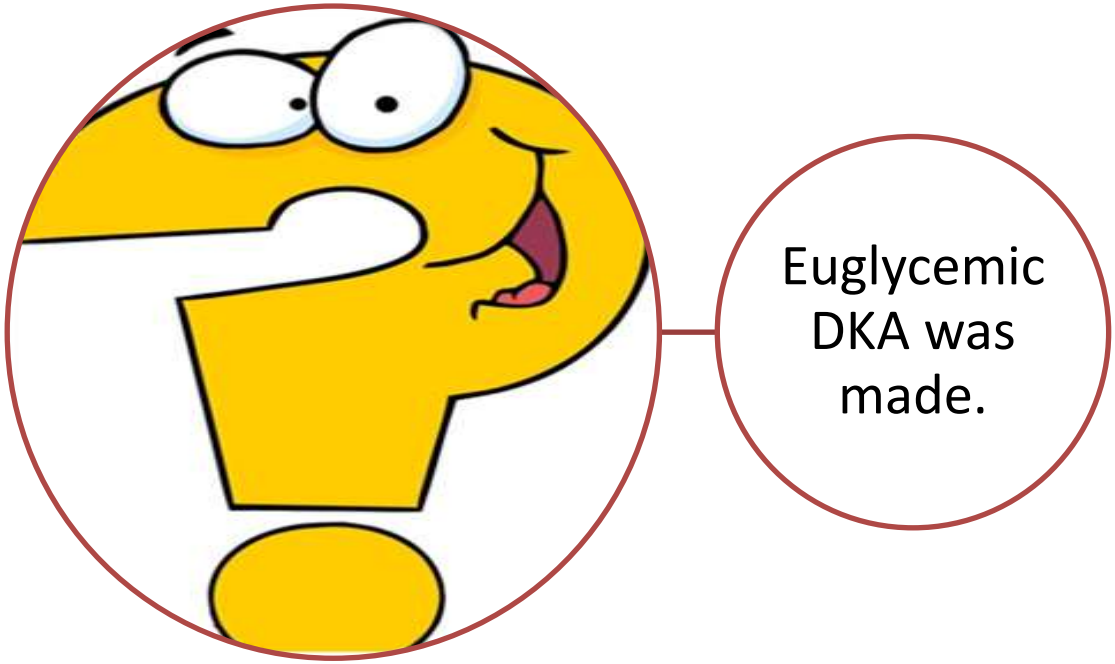
On admission

- BP 130/85 mmHg
- heart rate 130bpm
- respiratory rate 29

Laboratory findings

- a pH of 6.92
- pCO2 of 29 mm/hg
- HCO3 of 1.7 meq/L
- an anion gap of 23.
- serum glucose level measured 177mg/dl
- urine glucose level was 500 mg/dl along
- urine ketone levels greater than 150 mg/dl
- Leukocytosis with a count of 19,700 cm3

Diagnosis

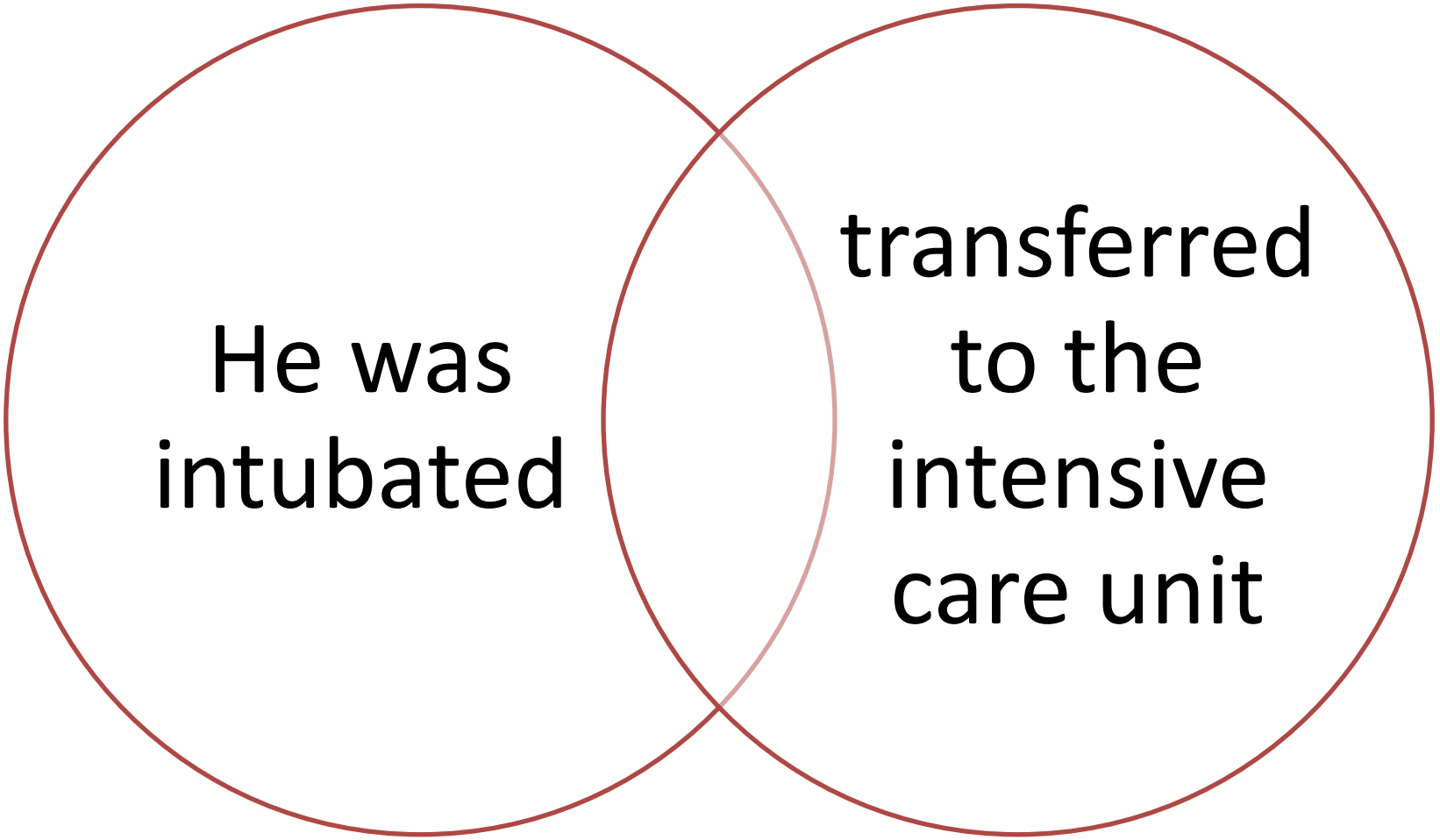

Euglycemic DKA was made.

Patient was initially treated

- intravenous fluid resuscitation with bicarbonate
- weight based subcutaneous insulin.
- Repeat ABGs showed worsening acidosis with pH of 6.85, pCO2 of 8mmhg, HCO3 of 1.3 meq/L.

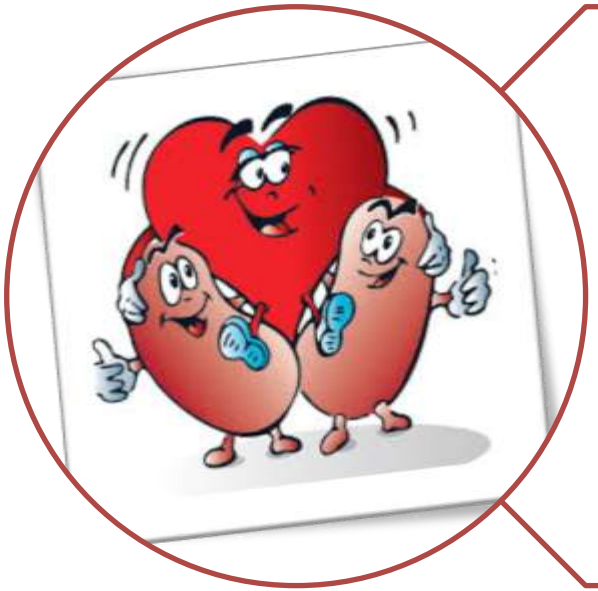
Then

- oliguric acute kidney injury with a creatinine of 4.5.
- tachypneic with a respiratory rate of 42
- lethargic
- nonresponsive.


He was intubated
transferred to the intensive care unit

He was started on

- insulin and bicarbonate drip
- Improvement of his metabolic acidosis
- renal function gradually worsened to a point where he needed intermittent hemodialysis.



Patient kidney function and respiratory status progressively improved and he was extubated on the day 6.

Table-1: Important labs from the date of admission to discharge

	0 hours	4 hours	8 hours	Day 2	Day 3	Day 4	Day 5	Day 6
pH	6.92	6.85	6.93	7.03	7.34	7.33	7.38	7.39
pCO2	9	8	8	23	26	26	31	36
HCO3	1.7	1.3	2	6	14	13	18	21
Glucose	178	110	264	195	219	182	137	126
Anion gap	30	25	16	13	6	10	11	12
Glucose	1.1	1.1	1.2	2.7	4.5	6.7	7.2	7.2
Creatinine	-	-	-	2.7	4.1	4.9	2.1	1.8

Type-1 diabetes mellitus (T1DM).

Euglycemic DKA has been defined as glucose levels <180 mg/dl and metabolic acidosis (serum bicarbonate <10 mEq/L).

Jenkins D, Close CF, Krentz AJ, Nattrass M, Wright AD. Euglycaemic diabetic ketoacidosis: does it exist? Acta Diabetol 1993;30(4):251–3.

Sodium-glucose cotransporter 2 (SGLT2) inhibitors, though FDA approved for type 2 diabetes mellitus (DM) only, are increasing being used off label as an adjunctive therapy to insulin in type-1 diabetics.

Euglycemic DKA and severe acute kidney injury requiring renal replacement therapy in a T1DM secondary to a SGLT 2 inhibitor (canagliflozin).

Henry RR, Rosenstock J, Chalamandaris AG, Kasichayanula S, Bogle A, Griffen SC. Exploring the potential of dapagliflozin in type 1 diabetes: Phase 2a pilot study. Diabetes 2013;62(Suppl 1):Abstract 70–LB.

Euglycemic DKA is a life threatening complication seen in both Types of diabetes mellitus, but its risk is much higher in T1DM as DKA is more commonly associated with T1DM.

Referral letter

- A 17 ys-old female with type 1 DM 9 years ago on insulin therapy presented with a 5-day history of facial swelling and right loin pain associated with a 2-day history of reduced urine output.

- Her blood pressures was 150/85 . In addition, her urine is dark in colour (the patient described it as “like coke’’. Urine dipstik showed pt+++, and blood++++ for renal team assessment .

How would you classify or describe her presentation?

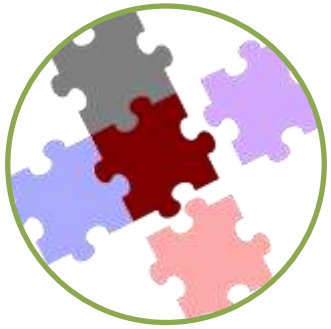
Typical feature of nephritic syndrome

- Acute renal dysfunction
- Micro/macroscopic hematuria
- Hypertension
- Protinuria
- edema

Laboratory investigation

- HB 11.5 g/dl
- WBCs 7.7 $x10^9$ /L
- PLT 289 $x10^9$ /L
- Na134 mmol/L
- K 5.6 mmol/L
- Sr cr was 0.9 mg/dl, then became 3.5 mg/dl at time of her referral
- ESR 46 mml/h
- CRP 49 mg/dl
- LFT normal
- HB a1c 7.1(FBS 110 mg/dl PPBS 145mg /dl)

- Urine dipistik pt+++, and hematuria ++++
- Urinary albumin 2.8 gm/d
- Dysmorphic urinary RBCs
- Chest x ray, and ECG were normal
- Renal US was completely normal (11.2 and 11.8) no backpressure, normal ecchogenicity and CMD.



AGN

The 52 year-old caucasian female patient suffered from reoccurring episodes of nausea and vomiting in the preceding days.

With a known history of type 1 diabetes, the patient was admitted to clinic in a state of severe hypoglycemia.

On admission

- elevated serum creatinine was noted, with creatinine levels initially being 3.6 mg/dl
- an estimated glomerular filtration rate (eGFR, according to the modified of diet in renal disease (MDRD) equation) of 13.3 ml/min/1.73 m2.

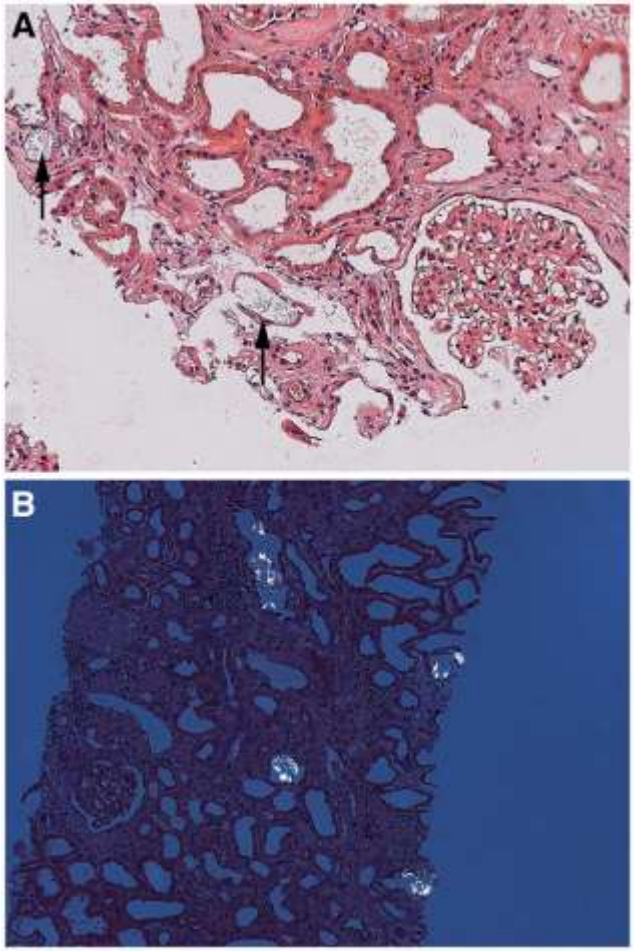
The patient was diagnosed with diabetes type 1 several years ago and has been treated with insulin on an intensified conventional therapy (ICT) regimen.

Previously, renal function was normal, with creatinine values remaining below 1.0 mg/dl, corresponding to a eGFR > 60 ml/min/1.73 m2 at routine consultations with her diabetologist.

A kidney biopsy was performed and showed mild diabetic mesangial sclerosis. Moreover, multiple birefringent crystallinous casts were found within the tubular lumen

Upon further questioning, the patient reported an increased ingestion of approximately 500 mg of rhubarb (fresh weight) per day in the last 4 weeks.

A) Oxalate crystals (arrows) within the renal tubular lumen in a hematoxylin eosin-stained section (original magnification x200) and (B) under polarisation light microscopy (original magnification x100). Adjacent glomeruli show mild diabetic mesangial sclerosis.



rhubarb (raw 805 mg/ 100 g FW, stewed 460 mg/100 g FW

Additional laboratory tests revealed elevated serum oxalate levels (13.75 µmol/l, reference range <6.5 µmol/l), whereas urinary excretion of oxalate, glycolate, citrate and calcium were normal

The history of high oxalate intake, the elevated serum oxalate levels, and the histological detection of intratubular birefringent crystals

lead to the diagnosis of secondary oxalosis, being the most likely cause for the acute decline in the patient`s renal function.

Acute renal failure in patients with type 1 diabetes mellitus

G. Woodrow, A.M. Brownjohn and J.H. Turney

Renal Unit, Leeds General Infirmary, Great George Street, Leeds LS1 3EX, UK

Postgrad Med J (1994) **70,** 192 – 194

Renal Unit, Leeds General Infirmary, Great George Street, Leeds LS1 3EX, UK

Between 1956 and 1992 a total of 1,661 patients with ARF (sudden deterioration of renal function or requiring dialysis in patients without previously known chronic renal impairment) were treated by the Renal Unit at Leeds General Infirmary.

26 patients from Renal Unit records who also had type 1 diabetes mellitus without previous evidence of chronic renal impairment.

23 of these patients with complete clinical details.

Diabetic ketoacidosis was the main underlying factor in 14 cases

Non-ketotic hyperosmolar coma was present in one

Three had severe sepsis (renal abscess, empyema and biliary disease)

Three had cardiac causes of ARF (myocardial infarction, cardiac failure and cardiac surgery)

One had pre-renal ARF due to Addison's disease presenting as fluid depletion and uraemia

The other occurred in a patient with a fractured femur and pre-existing cardiac failure.

Incidence and Characteristics of Acute Kidney Injury in Severe Diabetic Ketoacidosis

Jean-Christophe Orban[1,2*], Eve-Marie Maizière[1], Anis Ghaddab[1], Emmanuel Van Obberghen[2,3], Carole Ichai[1,2]

1 Réanimation médico-chirurgicale, Hôpital Saint-Roch, CHU de Nice, Nice, France, 2 IRCAN, Faculté de Médecine, Université de Nice Sophia-Antipolis, Nice, France, 3 Laboratoire de Biochimie, CHU de Nice, Nice, France

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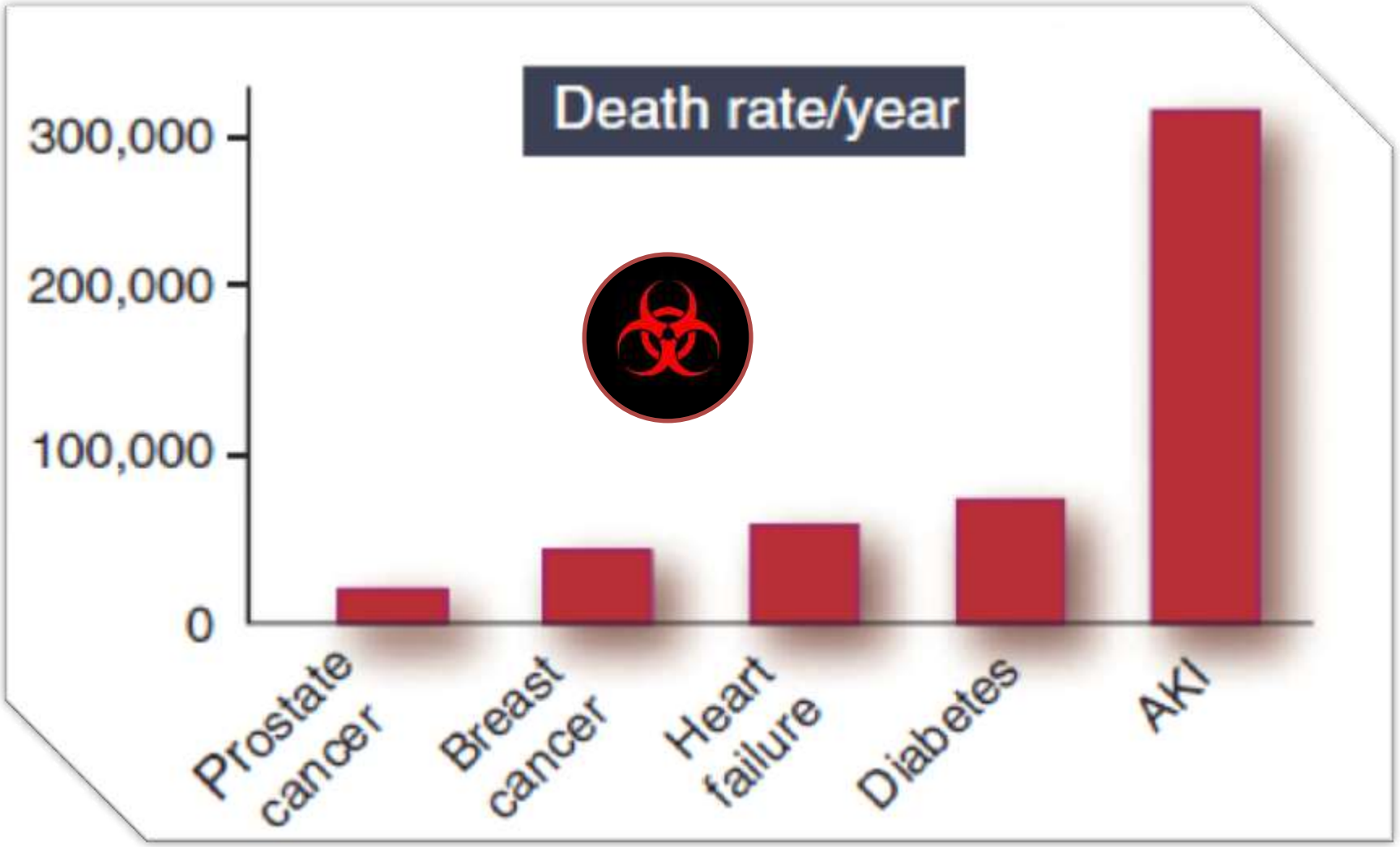
Conclusions

- Acute kidney injury is frequently associated with severe diabetic ketoacidosis on admission in ICU. Most of the time, this AKI is transient and characterised by a volume-responsiveness to fluid infusion used in DKA treatment. Age, blood glucose and serum protein are associated to the occurrence of AKI on ICU admission



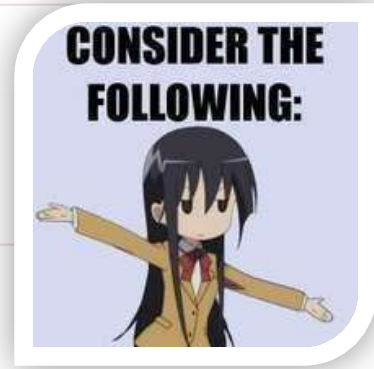
Kidney International advance online publication, 1 May 2013;

Definitions:

A rapid deterioration of parenchymal renal functions sufficiently severe to result in uremia.

- *Usually but not invariably reversible.*
- *Oliguria is usually, but not invariably a feature.*

Before 2004



FRONTIERS IN NEPHROLOGY

J Am Soc Nephrol 14: 2178–2187, 2003

Acute Renal Failure Definitions and Classification: Time for Change?

> 30 operational definitions of AKI

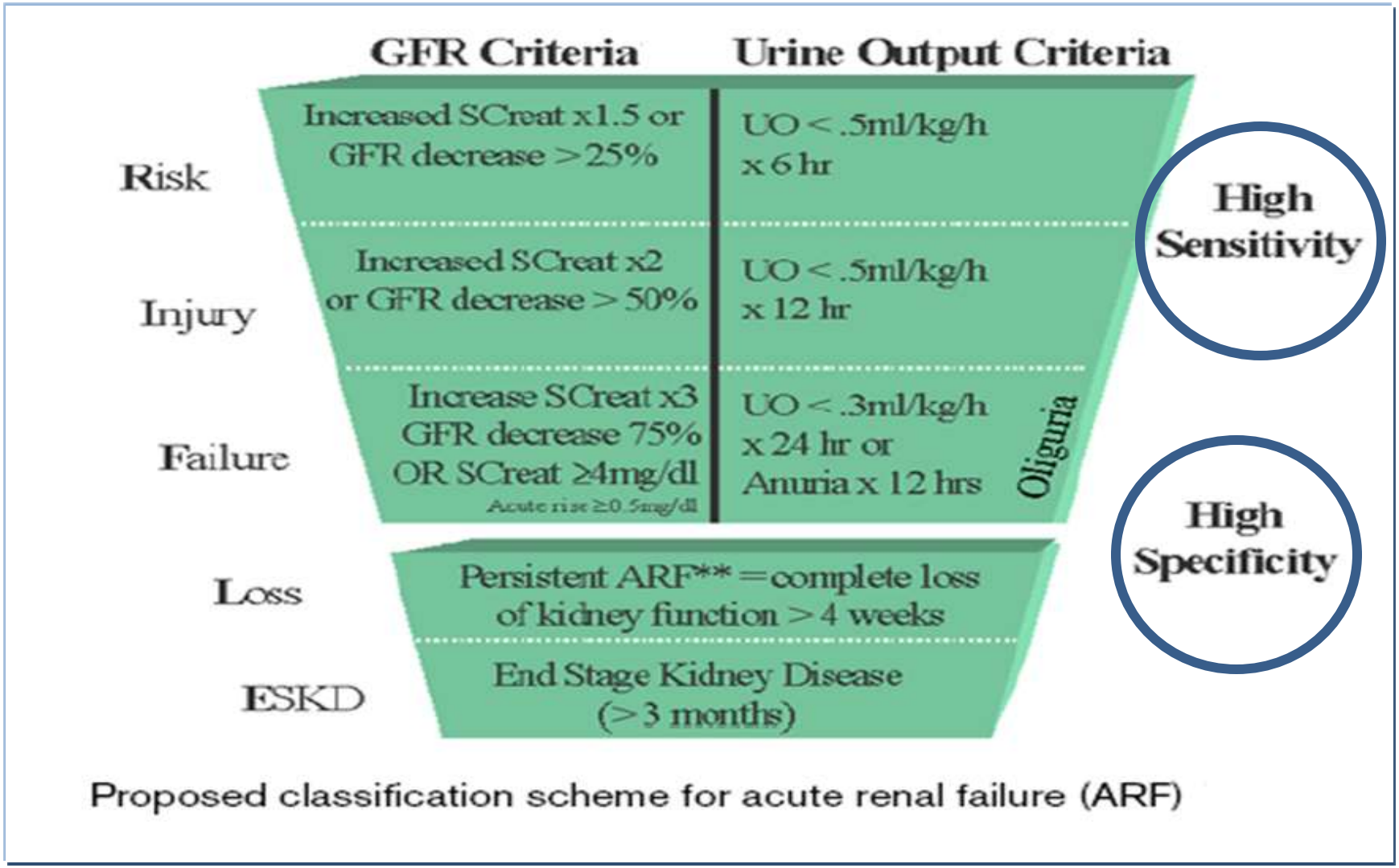
RAVINDRA L. MEHTA* and GLENN M. CHERTOW†

*Divisions of Nephrology, Departments of Medicine, *University of California San Diego and †University of California San Francisco, for the PICARD Study Group.*

RIFLE Birth

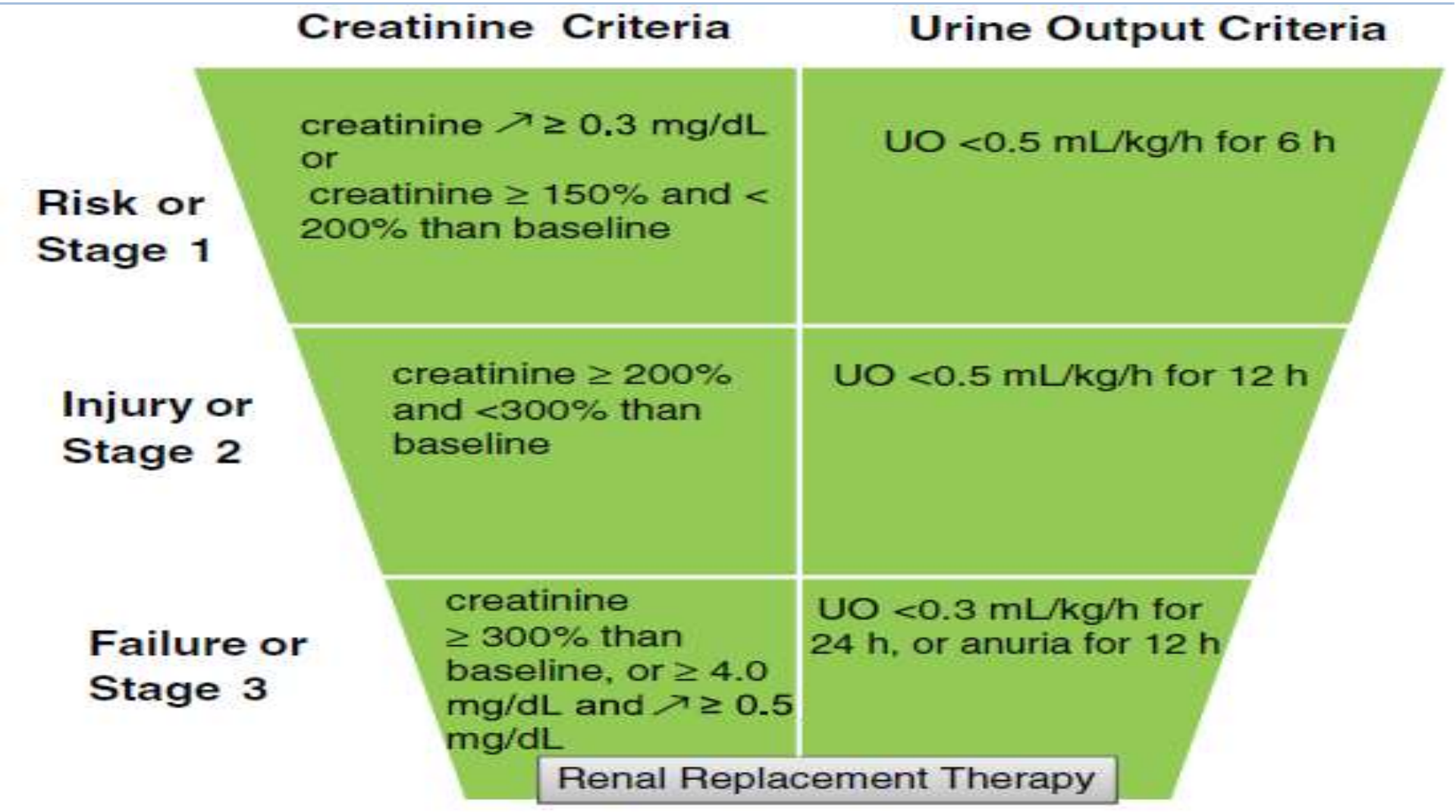
Crit Care 2004; 8: R204

RIFLE Classification



Proposed classification scheme for acute renal failure (ARF)

AKIN Classification



KDIGO Definition

2.1.2: AKI is staged for severity according to the following criteria. (*Not Graded*)

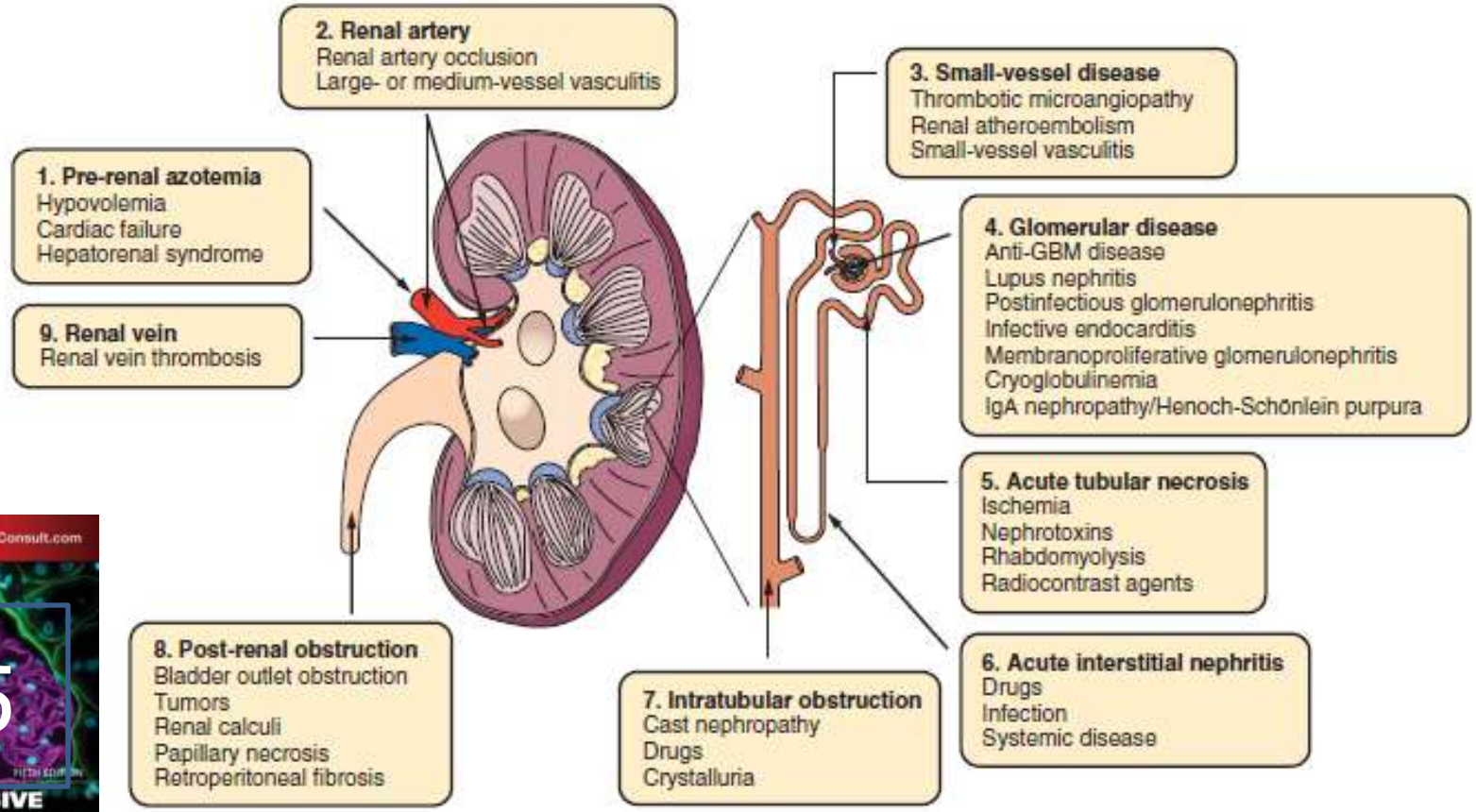
Stage 1: Increase in SCr by 1.5-1.9 times baseline; OR
Increase in sSCr by ≥0.3 mg/dL (≥26.5 μmol/L); OR
Urine output <0.5 mL/kg/h for 6-12 hours

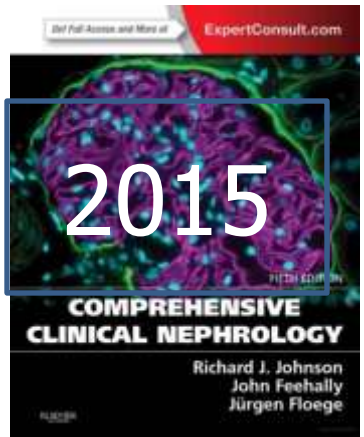
Stage 2: Increase in SCr by 2.0-2.9 times baseline; OR
Urine output <0.5 mL/kg/h for ≥12 hours

Stage 3: Increase in SCr by 3.0 times baseline; OR
Increase in SCr to 4.0 mg/dL (353.6 μmol/L); OR
Initiation of renal replacement therapy; OR
In patients <18 years, decrease in eGFR to 35 mL/min/1.73 m^2; OR
Urine output <0.3 mL/kg/h for ≥24 hours; OR
Anuria for ≥12 hours

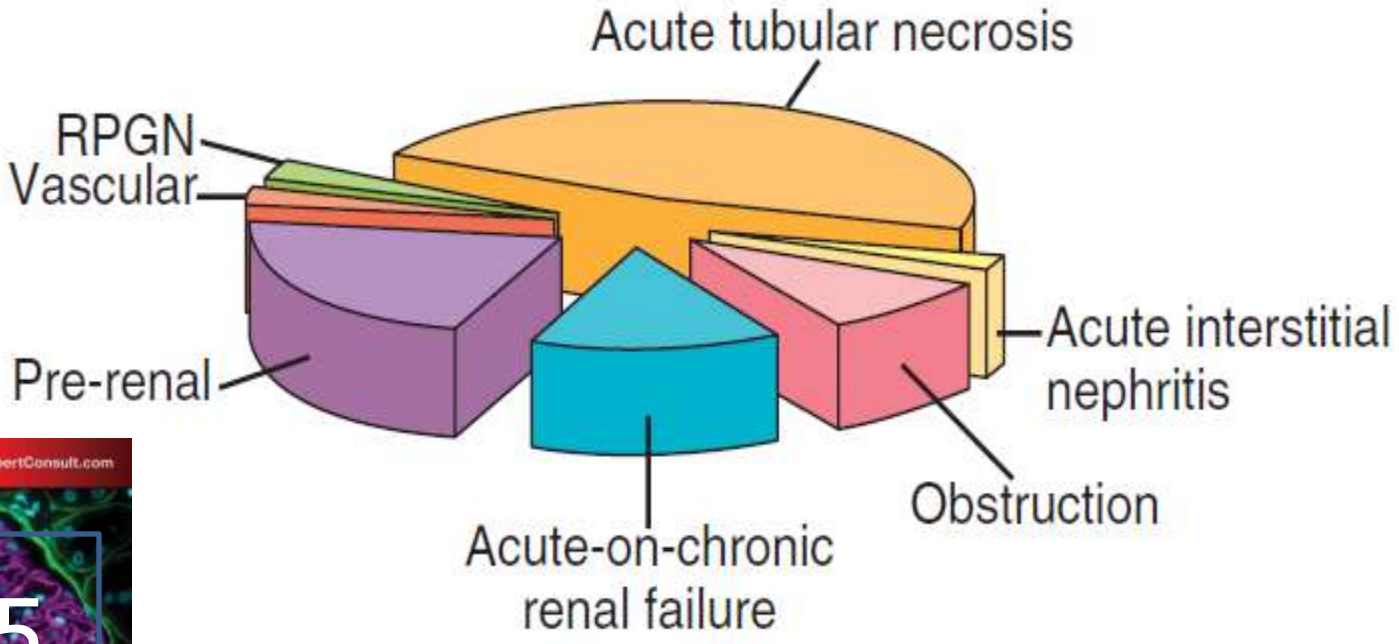
Kidney Int Suppl. 2012;2:1-138.

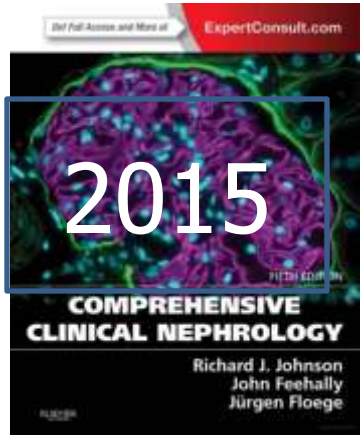
Etiology of AKI: An Overview





Etiology of AKI:
In The Hospital Settings





Pre-renal causes:

Any cause which results from kidney seeing to little blood flow

Volume deplete:

- GI
  - Vomiting
  - Diarrhea
- Bleeding
  - Trauma
  - Surgery
- Diuresis
  - Diabetes - DM, DI
  - Drugs

Kidney sees less volume:

- Sepsis
- CHF
- Cirrhosis
- Vascular - also consider in renal
  - RAS
  - Thrombus
  - Takayasu, PAN, KD
- Drugs
  - NSAIDs
  - ACEi
  - ARBs

Renal causes

Vascular:

Microvasculature:

- Sickle cell disease
- HUS
- Tumour lysis
- rhabdomyolysis

?Syndromes

- Hepatorenal
- Cardiorenal
- Pulmonary-renal

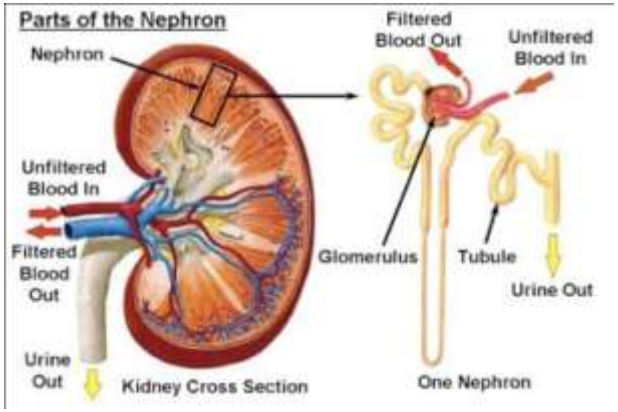
?Sepsis

inflamm, not all volume related

Glomerular:

Glomerulonephritis:

- Post-infectious
- membranoproliferative
- SLE
- HSP



Tubulo/Interstitial:

Acute tubular necrosis

-secondary to nephrotoxic insults or poor perfusion

Acute interstitial nephritis

-drugs

-infxn

Cortical dysplasia

-hypoxia/ischemia->infarct

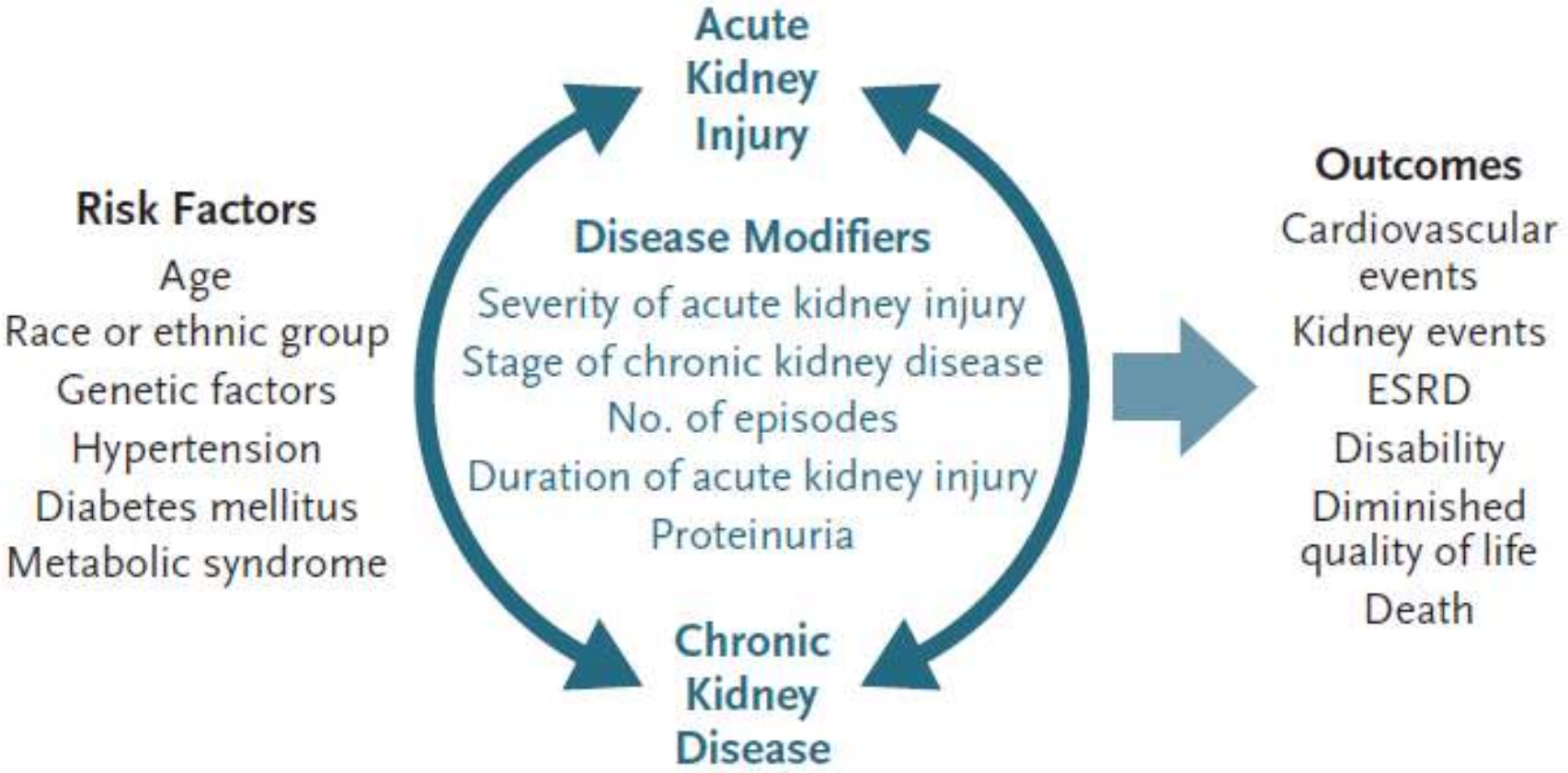
-toxins/severe HUS

Post-renal causes

Two kidneys - distal or bilateral proximal obstruction

Single kidney - obstruction anywhere

- Posterior urethral valves
- Ureteropelvic junction obstruction
- Ureterovesicular junction obstruction
- Ureterocele
- Stones
- Tumour
- Hemorrhagic cystitis
- Neurogenic bladder



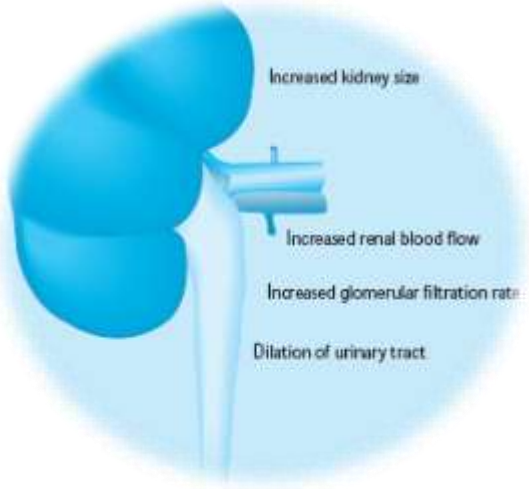
N Engl J Med July 3rd, 2014;371:58-66.

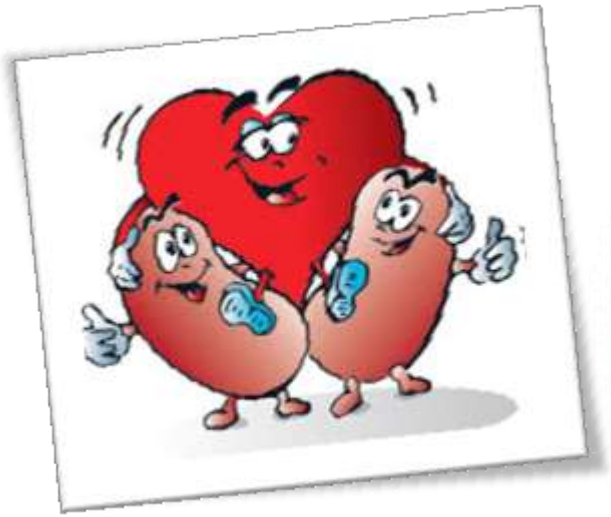
Prevention of AKI in ICU

- Recognition of underlying risk factors
  - Diabetes
  - CKD
  - Age
  - HTN
  - Cardiac/liver dysfunction
- Maintenance of renal perfusion
- Avoidance of hyperglycemia
- Avoidance of nephrotoxins

Dennen P, Douglas I, Anderson R,: Acute Kidney Injury in the Intensive Care Unit: An update and primer for the Intensivist. *Critical Care Medicine* 2010; 38:261-275.

- DM is a risk factor for AKI
- DKA is the commonest cause of AKI in type 1 DM
- Early detection and prevention of AKI is the future target of TTT





Mansoura Nephrology and Dialysis unit

MNDU

A great man once said, "*Everything is possible. The impossible just takes longer…*"